

WHAT IS CLAIMED IS:

1. An antibody mutant of a species-dependent antibody, which antibody mutant comprises an amino acid substitution in a hypervariable region of the species-dependent antibody and has a binding affinity for an antigen from a nonhuman mammal which is at least about 10 fold stronger than the binding affinity of the species-dependent antibody for said antigen.
2. The antibody mutant of claim 1 wherein the species-dependent antibody binds specifically to the human homologue of said antigen.
3. The antibody mutant of claim 1 wherein the antibody mutant is to be administered to a nonhuman mammal in preclinical studies.
4. The antibody mutant of claim 1 wherein the nonhuman mammal is a primate.
5. The antibody mutant of claim 4 wherein the nonhuman primate is selected from the group consisting of rhesus, cynomolgus, baboon, chimpanzee and macaque.
6. The antibody mutant of claim 1 wherein only one hypervariable region residue of the species-dependent antibody has been substituted.
7. The antibody mutant of claim 1 wherein two to ten hypervariable region residues of the species-dependent antibody have been substituted.
8. The antibody mutant of claim 1 wherein the antibody mutant has a binding affinity for said antigen from the nonhuman mammal which is at least about 20 fold stronger than the binding affinity of the species-dependent antibody for said antigen.
9. The antibody mutant of claim 1 wherein the antibody mutant has a binding affinity for said antigen from the nonhuman mammal which is at least about 50 fold stronger than the binding affinity of the species-dependent antibody for said antigen.

10. The antibody mutant of claim 1 further comprising an amino acid substitution in a framework region of said species-dependent antibody.
11. The antibody mutant of claim 1 wherein the species-dependent antibody is a humanized antibody.
12. The antibody mutant of claim 1 wherein the species-dependent antibody is a human antibody.
13. The antibody mutant of claim 1 which comprises a heavy chain variable domain comprising the amino acid sequence in SEQ ID NO:17. ✓
14. A method for producing an antibody mutant comprising substituting an amino acid residue in a hypervariable region of a species-dependent antibody, wherein the antibody mutant has a binding affinity for an antigen from a nonhuman mammal which is at least about 10 fold stronger than the binding affinity of the species-dependent antibody for said antigen.
15. The method of claim 14 wherein the substituted amino acid residue is one which has been identified as being involved in binding the antigen is from the nonhuman mammal.
16. The method of claim 14 wherein the substituted amino acid residue is one which has been identified as being involved in binding a homologue of the antigen from the mammal, where the homologue is from a human.
17. A method for making an antibody mutant, comprising the steps of: ↗
(a) identifying hypervariable region residues in a species-dependent antibody which are involved in binding an antigen from a first mammalian species and those hypervariable region residues involved in binding a homologue of the antigen from a second different mammalian species;

(b) preparing a mutant of the species-dependent antibody wherein a residue identified in (a) as being involved in binding the antigen from the first mammalian species or the homologue thereof, or both, is replaced by another amino acid residue; and

(c) selecting an antibody mutant prepared as in (b) which has a stronger binding affinity for the antigen from the second mammalian species than the species-dependent antibody.

18. The method of claim 17 wherein the first mammalian species is a human.

19. The method of claim 17 wherein the second mammalian species is a nonhuman mammal.

20. The method of claim 17 wherein step (b) involves preparing a mutant of the species-dependent antibody wherein a residue identified in (a) as being involved in binding the homologue, but not the antigen from the first mammalian species, is replaced by another amino acid residue.

21. The method of claim 17 wherein step (b) involves preparing a mutant of the species-dependent antibody wherein a residue identified in (a) as being involved in binding both the antigen from the first mammalian species and the homologue thereof is replaced by another amino acid residue.

22. The method of claim 17 wherein step (b) involves preparing a mutant of the species-dependent antibody wherein a residue identified in (a) as being involved in binding the antigen from the first mammalian species, but not the homologue thereof, is replaced by another amino acid residue.

23. Isolated nucleic acid encoding the antibody mutant of claim 1.

24. A vector comprising the nucleic acid of claim 23.

25. A host cell transformed with the vector of claim 24.

26. A process of producing an antibody mutant comprising culturing the host cell of claim 25 so that the nucleic acid is expressed.

27. The process of claim 26 further comprising recovering the antibody mutant from the host cell culture.

28. The process of claim 27 wherein the antibody mutant is recovered from the host cell culture medium.